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OXIDATIVE DECARBOXYLATION OF α-KETO CARBOXYLIC ACIDS BY CARBONYL OXIDES

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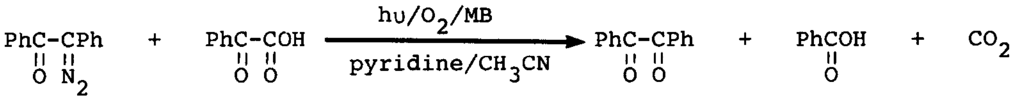
Abstract: Photosensitized oxygenation of α-keto carboxylic acids in the presence of diazo compounds afforded the corresponding carboxylic acids and carbon dioxide in high yields; oxidative decarboxylation by carbonyl oxides occurred.

Hydroxylations catalyzed by several dioxygenases require α-keto carboxylic acid as co-factor. Half a mole of molecular oxygen is introduced into substrate (S-H) while the other half is taken up by the α-keto carboxylic acid which undergoes oxidative decarboxylation; in this system the α-keto carboxylic acid acts as oxygen atom acceptor.[1)]

$$\text{S-H} + O_2 + RCOCO_2H \xrightarrow{\text{Dioxygenase}} \text{S-OH} + RCO_2H + CO_2$$

Several enzymatic model reactions have been reported for the conversion of α-keto carboxylic acids into the corresponding carboxylic acids and carbon dioxide. These reactions proceed by singlet oxygen[2,3,4)], superoxide[5)], iodosobenzene[6)], and Fe^{2+}/H_2O_2.[7)] Many enzymatic oxygenations are conveniently explained in term of oxenoid reagents. Chemical systems which can function as active oxygen atom transfer agents are carbonyl oxide[8)], pyridine N-oxides[9)], selenium oxides[10)], and the intermediate formed in the metal ion catalyzed oxygenation of azibenzil.[11)] The unique reactivity of carbonyl oxides promped us to examine the decarboxylation of α-keto carboxylic acids by carbonyl oxides with the aim of clarifying its role as an oxidant in biological systems. We now report the first successful example of this new type of decarboxylation.

Carbonyl oxides were generated by photosensitized oxygenation of diazo compounds (1 and 2) in pyridine-acetonitrile. In a typical reaction, a solution of phenylglyoxylic acid (3 mmol) in acetonitrile (10 ml) and pyridine (3 ml) was added to the solution of benzoylphenyldiazomethane (1, 1 mmol) in acetonitrile (20 ml); the resulting solution was irradiated by a 500 W Halogen lamp while passing oxygen for 80 mins. using methylene blue as sensitizer. After methylation with excess diazomethane in ether, the products were directly analyzed by glc. Methyl benzoate and benzil were obtained in 88 and 90 % yields, respectively, together with carbon dioxide in 80 % yield based on benzoylphenyldiazomethane. When the diazo compound

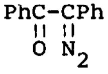
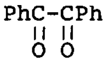
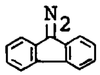
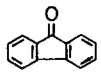


$$\mathrm{Ph}\underset{\mathrm{O}}{\underset{\|}{\mathrm{C}}}\text{-}\underset{\mathrm{N_2}}{\underset{\|}{\mathrm{C}}}\mathrm{Ph} + \mathrm{Ph}\underset{\mathrm{O}}{\underset{\|}{\mathrm{C}}}\text{-}\underset{\mathrm{O}}{\underset{\|}{\mathrm{C}}}\mathrm{OH} \xrightarrow[\text{pyridine/CH}_3\text{CN}]{h\nu/\mathrm{O_2}/\mathrm{MB}} \mathrm{Ph}\underset{\mathrm{O}}{\underset{\|}{\mathrm{C}}}\text{-}\underset{\mathrm{O}}{\underset{\|}{\mathrm{C}}}\mathrm{Ph} + \mathrm{Ph}\underset{\mathrm{O}}{\underset{\|}{\mathrm{C}}}\mathrm{OH} + \mathrm{CO_2}$$

1 90 % 88 % 80 %

was absent, decarboxylation by dye sensitization alone was less than 14 % under the conditions used.[12] In the absence of pyridine, α-keto carboxylic acids react with diazo compounds (1 and 2) to give only the corresponding esters[13], and the parent carboxylic acids were not obtained under the oxidation conditions. These results suggest that the carbonyl oxides are acting as an oxygen atom transfer agent. The results are summarized in Table. In contrast to α-keto carboxylic acids α-keto ester is inert to carbonyl oxide. Although the present data shows that the carbonyl oxide certainly causes oxidative decarboxylation of α-keto carboxylic acids, we in no way wish to infer that this is actually occurring in enzymatic process; however we believe that these findings may provide an useful mechanistic insight into this important and complex process.

Table. Photosensitized Oxygenation of α-Keto Carboxylic Acids in the Presence of Diazo Compounds.[a)]

Diazo compd.	α-Keto acid	Products and Yields[b,c)]			
(1 mmol)	(3 mmol)	Acid		Ketone	
 $\overset{\displaystyle\text{PhC}}{\underset{\text{O}}{\Vert}}-\overset{\displaystyle\text{CPh}}{\underset{\text{N}_2}{\Vert}}$ 1	$PhCOCO_2H$	$PhCO_2H$	88 %[d)]	 $\overset{\displaystyle\text{PhC}}{\underset{\text{O}}{\Vert}}-\overset{\displaystyle\text{CPh}}{\underset{\text{O}}{\Vert}}$	90 %
	$PhCOCO_2Et$	$PhCO_2H$	0		94
	CH_3COCO_2H	CH_3CO_2H	96		100
	$CH_3CH_2COCO_2H$	$CH_3CH_2CO_2H$	64		95
	$CH_3(CH_2)_2COCO_2H$	$CH_3(CH_2)_2CO_2H$	65		97
	$HO_2C(CH_2)_2COCO_2H$	$HO_2C(CH_2)_2CO_2H$	66[d)]		91
 2	$PhCOCO_2H$	$PhCO_2H$	82[d)]		97
	CH_3COCO_2H	CH_3CO_2H	65		93
	$CH_3CH_2COCO_2H$	$CH_3CH_2CO_2H$	68		98
	$CH_3(CH_2)_2COCO_2H$	$CH_3(CH_2)_2CO_2H$	66		90
	$HO_2C(CH_2)_2COCO_2H$	$HO_2C(CH_2)_2CO_2H$	43[d)]		83

a) The reactions were carried out using 500 W Halogen lamp at water temperature for 80 min.

b) The yields were determined based on diazo compounds used.

c) The other product of the reaction was CO_2 which was detected by precipitation of barium carbonate by passing exite gases through aqueous barium hydroxide.

d) Determined as a methyl ester.

Mechanistic study for the decarboxylation is currently in progress.

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References and Notes.

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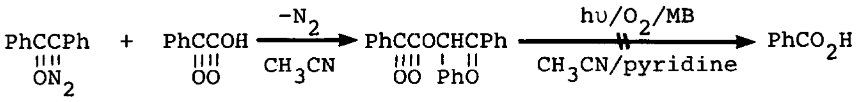
12) Decarboxylation by carbonyl oxides was very fast compared with dye sensitized oxygenation. Phenylglyoxylic acid is inert to dye sensitized oxygenation. See ref. 2.
13) Reaction of benzoylphenyldiazomethane with phenyl glyoxylic acid is illustrated.



$$\mathrm{Ph\underset{O}{C}\underset{N_2}{C}Ph} + \mathrm{Ph\underset{O}{C}\underset{O}{C}OH} \xrightarrow[\mathrm{CH_3CN}]{-\mathrm{N_2}} \mathrm{Ph\underset{O}{C}\underset{O}{C}O\underset{Ph}{CH}\underset{O}{C}Ph} \not\xrightarrow[\mathrm{CH_3CN/pyridine}]{h\nu/\mathrm{O_2/MB}} \mathrm{PhCO_2H}$$

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